

WHAT IS CLAIMED IS:

1. An isolated protein complex having a first protein which is Tsg101 or a homologue or derivative or fragment thereof interacting with a second protein which is HIV GAG polypeptide or a homologue or derivative or fragment thereof.

2. The isolated protein complex of Claim 1, wherein said second protein is HIV GAGp6 or a fragment thereof.

3. The isolated protein complex of Claim 1, wherein said first protein is a fusion protein containing (a) Tsg101 or (b) a Tsg101 homologue or (c) a Tsg101 fragment.

4. The isolated protein complex of Claim 1, wherein said second protein is a fusion protein containing (a) HIV GAG polypeptide or (b) a HIV GAG homologue or (c) a HIV GAG fragment.

5. An isolated protein complex having a first protein which is Tsg101 or a homologue or derivative or fragment thereof interacting with a second protein which is HIV GAGp6 polypeptide or a homologue or derivative or fragment thereof.

6. The isolated protein complex of Claim 5, wherein said first protein is a fusion protein containing (a) Tsg101 or (b) a Tsg101 homologue or (c) a Tsg101 fragment.

7. The isolated protein complex of Claim 5, wherein said second protein is a fusion protein containing (a) HIV GAGp6 polypeptide or (b) a HIV GAGp6 homologue or (c) a HIV GAGp6 fragment.

8. An isolated protein complex comprising:

- (a) a first protein which is selected from group consisting of
  - (i) Tsg101 protein,

(ii) a Tsg101 protein homologue having an amino acid sequence at least 90% identical to that of Tsg101 and capable of interacting with HIV GAGp6,

(iii) a Tsg101 protein fragment containing the Tsg101 UEV domain, and

(iv) a fusion protein containing said Tsg101 protein, said Tsg101 protein homologue or said Tsg101 protein fragment; and

(b) a second protein selected from the group consisting of

(1) HIV GAG polypeptide,

(2) a HIV GAG polypeptide homologue having an amino acid sequence at least 90% identical to that of HIV GAG polypeptide and capable of interacting with Tsg101,

(3) HIV GAGp6 protein,

(4) a HIV GAGp6 homologue having an amino acid sequence at least 90% identical to that of HIV GAGp6 polypeptide and capable of interacting with Tsg101,

(5) a HIV GAGp6 fragment capable of interacting with Tsg101, and

(6) a fusion protein containing said HIV GAG polypeptide, said HIV GAG polypeptide homologue, said HIV GAGp6 protein, said HIV GAGp6 homologue or said HIV GAGp6 fragment.

9. The isolated protein complex of Claim 8, wherein said HIV GAGp6 fragment contains an amino acid sequence of SEQ ID NO:25 or SEQ ID NO:26.

10. The isolated protein complex of Claim 8, wherein said HIV GAGp6 fragment contains an amino acid sequence of SEQ ID NO:31 or SEQ ID NO:32.

11. The isolated protein complex of Claim 8, wherein said HIV GAGp6 fragment has a contiguous span of at least 10 amino acid residues of a naturally occurring HIV GAGp6, said contiguous span containing a P(T/S)AP late domain motif.

12. An isolated protein complex comprising a first protein which is Tsg101 or a homologue or derivative or fragment thereof interacting with a second protein which is

a retrovirus GAG polypeptide containing the P(T/S)AP late domain motif or a homologue or derivative or fragment of said retrovirus GAG polypeptide.

13. The isolated protein complex of Claim 12, wherein said retrovirus is a lentivirus.

14. The isolated protein complex of Claim 13, wherein said lentivirus is a primate lentivirus.

15. The isolated protein complex of Claim 14, wherein said primate lentivirus is selected from the group consisting of HIV-1, HIV-2, HIV-3, and simian immunodeficiency viruses.

16. The isolated protein complex of Claim 13, wherein said lentivirus is a non-primate lentivirus selected from the group consisting of bovine lentiviruses, feline lentiviruses, and ovine/caprine lentiviruses.

17. An isolated protein complex comprising:

- (a) a first protein which is selected from group consisting of
  - (i) Tsg101 protein,
  - (ii) a Tsg101 protein homologue having an amino acid sequence at least 90% identical to that of Tsg101 and capable of interacting with HIV GAGp6,
  - (iii) a Tsg101 protein fragment containing the Tsg101 UEV domain, and
  - (iv) a fusion protein containing said Tsg101 protein, said Tsg101 protein homologue or said Tsg101 protein fragment; and
- (b) a second protein selected from the group consisting of
  - (1) a retrovirus GAG polypeptide having the P(T/S)AP late domain motif,
  - (2) a homologue of said retrovirus GAG polypeptide, said homologue having an amino acid sequence at least 90% identical to that of said retrovirus GAG polypeptide and capable of interacting with Tsg101,

(3) a fragment of said retrovirus GAG polypeptide, said fragment being capable of interacting with Tsg101, and

(4) a fusion protein containing said retrovirus GAG polypeptide, said retrovirus GAG polypeptide homologue or said retrovirus GAG polypeptide fragment.

18. The isolated protein complex of Claim 17, wherein said retrovirus is a lentivirus.

19. The isolated protein complex of Claim 18, wherein said lentivirus is a primate lentivirus.

20. The isolated protein complex of Claim 19, wherein said primate lentivirus is selected from the group consisting of HIV-1, HIV-2, HIV-3, and simian immunodeficiency viruses.

21. The isolated protein complex of Claim 19, wherein said lentivirus is a non-primate lentivirus selected from the group consisting of bovine lentiviruses, feline lentiviruses, and ovine/caprine lentiviruses.

22. An isolated protein complex comprising:

- (a) a first protein which is selected from group consisting of
  - (i) Tsg101 protein,
  - (ii) a Tsg101 protein homologue having an amino acid sequence at least 90% identical to that of Tsg101 and capable of interacting with HIV GAGp6,
  - (iii) a Tsg101 protein fragment containing the Tsg101 UEV domain, and
  - (iv) a fusion protein containing said Tsg101 protein, said Tsg101 protein homologue or said Tsg101 protein fragment; and
- (b) a second protein selected from the group consisting of
  - (1) a primate lentivirus GAG polypeptide,
  - (2) a primate lentivirus GAG polypeptide homologue having an amino

acid sequence at least 90% identical to that of said primate lentivirus GAG polypeptide and capable of interacting with Tsg101,

- (3) a primate lentivirus GAGp6 protein,
- (4) a primate lentivirus GAGp6 homologue having an amino acid sequence at least 90% identical to that of HIV GAGp6 polypeptide and capable of interacting with Tsg101,
- (5) a primate lentivirus GAGp6 fragment capable of interacting with Tsg101, and

(6) a fusion protein containing said primate lentivirus GAG polypeptide, said primate lentivirus GAG polypeptide homologue, said primate lentivirus GAGp6 protein, said primate lentivirus GAGp6 homologue or said primate lentivirus GAGp6 fragment.

23. An isolated protein complex comprising:  
a first fusion protein having a Tsg101 protein fragment interacting with  
a second fusion protein containing a fragment of HIV GAG polypeptide.

24. A method for making the protein complex of Claim 1, comprising the steps of:

providing said first protein and said second protein; and  
contacting said first protein with said second protein.

25. A protein microarray comprising the protein complex according to Claim 1.

26. A fusion protein having a first polypeptide covalently linked to a second polypeptide, wherein said first polypeptide is Tsg101 or a homologue or fragment thereof, and wherein said second polypeptide is HIV GAGp6 or a homologue or fragment thereof.

27. An isolated nucleic acid encoding the fusion protein of Claim 26.

28. A method for selecting modulators of a protein complex according to Claim 8, comprising:

providing the protein complex;  
contacting said protein complex with a test compound; and  
determining the presence or absence of binding of said test compound to said protein complex.

29. A method for selecting modulators of an interaction between a first protein and a second protein,

(a) said first protein being selected from group consisting of  
(i) Tsg101 protein,  
(ii) a Tsg101 protein homologue having an amino acid sequence at least 90% identical to that of Tsg101 and capable of interacting with HIV GAGp6,  
(iii) a Tsg101 protein fragment containing the Tsg101 UEV domain, and  
(iv) a fusion protein containing said Tsg101 protein, said Tsg101 protein homologue or said Tsg101 protein fragment; and  
(b) said second protein being selected from the group consisting of  
(1) HIV GAG polypeptide,  
(2) a HIV GAG polypeptide homologue having an amino acid sequence at least 90% identical to that of HIV GAG polypeptide and capable of interacting with Tsg101,  
(3) HIV GAGp6 protein,  
(4) a HIV GAGp6 homologue having an amino acid sequence at least 90% identical to that of HIV GAGp6 polypeptide and capable of interacting with Tsg101,  
(5) a HIV GAGp6 fragment capable of interacting with Tsg101, and  
(6) a fusion protein containing said HIV GAG polypeptide, said HIV GAG polypeptide homologue, said HIV GAGp6 protein, said HIV GAGp6 homologue or said HIV GAGp6 fragment, said method comprising:  
contacting said first protein with said second protein in the presence of one or more test compounds; and

determining the interaction between said first protein and said second protein.

30. The method of Claim 29, wherein at least one of said first and second proteins is a fusion protein having a detectable tag.

31. The method of Claim 29, wherein said contacting step is conducted in a substantially cell free environment.

32. The method of Claim 29, wherein said contacting step is conducted in a host cell.

33. The method of Claim 32, wherein said host cell is a yeast cell.

34. A method for selecting modulators of an interaction between a first protein and a second protein,

(a) said first protein being selected from group consisting of

(i) Tsg101 protein,

(ii) a Tsg101 protein homologue having an amino acid sequence at least 90% identical to that of Tsg101 and capable of interacting with HIV GAGp6,

(iii) a Tsg101 protein fragment containing the Tsg101 UEV domain, and

(iv) a fusion protein containing said Tsg101 protein, said Tsg101 protein homologue or said Tsg101 protein fragment; and

(b) said second protein being selected from the group consisting of

(1) a retrovirus GAG polypeptide having the P(T/S)AP late domain motif,

(2) a homologue of said retrovirus GAG polypeptide, said homologue having an amino acid sequence at least 90% identical to that of said retrovirus GAG polypeptide and capable of interacting with Tsg101,

(3) a fragment of said retrovirus GAG polypeptide, said fragment being capable of interacting with Tsg101, and

(4) a fusion protein containing said retrovirus GAG polypeptide, said

retrovirus GAG polypeptide homologue or said retrovirus GAG polypeptide fragment, said method comprising:

contacting said first protein with said second protein in the presence of one or more test compounds; and

determining the interaction between said first protein and said second protein.

35. The method of Claim 34, wherein said contacting step is conducted in a substantially cell free environment.

36. The method of Claim 34, wherein said contacting step is conducted in a host cell.

37. A method for selecting modulators of the protein complex of Claim 8, comprising:

contacting said protein complex with a test compound; and

determining the interaction between said first protein and said second protein.

38. A method for selecting modulators of the protein complex of Claim 17, comprising:

contacting said protein complex with a test compound; and

determining the interaction between said first protein and said second protein.

39. A method for selecting modulators of the protein complex of Claim 22, comprising:

contacting said protein complex with a test compound; and

determining the interaction between said first protein and said second protein.

40. A method for selecting modulators of an interaction between a first polypeptide and a second polypeptide,

(a) said first polypeptide being selected from group consisting of

(i) Tsg101 protein,

(ii) a Tsg101 protein homologue having an amino acid sequence at least 90% identical to that of Tsg101 and capable of interacting with HIV GAGp6, and  
(iii) a Tsg101 protein fragment containing the Tsg101 UEV domain; and  
(b) said second polypeptide being selected from the group consisting of  
(1) HIV GAG polypeptide,  
(2) a HIV GAG polypeptide homologue having an amino acid sequence at least 90% identical to that of HIV GAG polypeptide and capable of interacting with Tsg101,  
(3) HIV GAGp6 protein,  
(4) a HIV GAGp6 homologue having an amino acid sequence at least 90% identical to that of HIV GAGp6 polypeptide and capable of interacting with Tsg101, and  
(5) a HIV GAGp6 fragment capable of interacting with Tsg101, said method comprising:

providing in a host cell a first fusion protein having said first polypeptide, and a second fusion protein having said second polypeptide, wherein a DNA binding domain is fused to one of said first and second polypeptides while a transcription-activating domain is fused to the other of said first and second polypeptides;

providing in said host cell a reporter gene, wherein the transcription of the reporter gene is determined by the interaction between the first polypeptide and the second polypeptide;

allowing said first and second fusion proteins to interact with each other within said host cell in the presence of a test compound; and

determining the presence or absence of expression of said reporter gene.

41. The method of Claim 40, wherein said host cell is a yeast cell.

42. A method for selecting modulators of the protein complex of Claim 17, comprising:

providing in a host cell a first fusion protein containing said first protein, and a second fusion protein containing said second protein, wherein a DNA binding domain is

fused to one of said first and second polypeptides while a transcription-activating domain is fused to the other of said first and second proteins;

providing in said host cell a reporter gene, wherein the transcription of the reporter gene is determined by the interaction between the first protein and the second protein;

allowing said first and second fusion proteins to interact with each other within said host cell in the presence of a test compound; and

determining the presence or absence of expression of said reporter gene.

43. A method for selecting modulators of the protein complex of Claim 22, comprising:

providing in a host cell a first fusion protein containing said first protein, and a second fusion protein containing said second protein, wherein a DNA binding domain is fused to one of said first and second polypeptides while a transcription-activating domain is fused to the other of said first and second proteins;

providing in said host cell a reporter gene, wherein the transcription of the reporter gene is determined by the interaction between the first protein and the second protein;

allowing said first and second fusion proteins to interact with each other within said host cell in the presence of a test compound; and

determining the presence or absence of expression of said reporter gene.

44. A composition comprising:

(a) a first expression vector having a nucleic acid encoding a first protein which is selected from group consisting of

(i) Tsg101 protein,

(ii) a Tsg101 protein homologue having an amino acid sequence at least 90% identical to that of Tsg101 and capable of interacting with HIV GAGp6,

(iii) a Tsg101 protein fragment containing the Tsg101 UEV domain, and

(iv) a fusion protein containing said Tsg101 protein, said Tsg101 protein homologue or said Tsg101 protein fragment; and

(b) a second expression vector having a nucleic acid encoding a second protein selected from the group consisting of

- (1) HIV GAG polypeptide,
- (2) a HIV GAG polypeptide homologue having an amino acid sequence at least 90% identical to that of HIV GAG polypeptide and capable of interacting with Tsg101,
- (3) HIV GAGp6 protein,
- (4) a HIV GAGp6 homologue having an amino acid sequence at least 90% identical to that of HIV GAGp6 polypeptide and capable of interacting with Tsg101,
- (5) a HIV GAGp6 fragment capable of interacting with Tsg101, and
- (6) a fusion protein containing said HIV GAG polypeptide, said HIV GAG polypeptide homologue, said HIV GAGp6 protein, said HIV GAGp6 homologue or said HIV GAGp6 fragment.

45. A host cell comprising:

(a) a first expression vector having a nucleic acid encoding a first protein which is selected from group consisting of

- (i) Tsg101 protein,
- (ii) a Tsg101 protein homologue having an amino acid sequence at least 90% identical to that of Tsg101 and capable of interacting with HIV GAGp6,
- (iii) a Tsg101 protein fragment containing the Tsg101 UEV domain, and
- (iv) a fusion protein containing said Tsg101 protein, said Tsg101 protein homologue or said Tsg101 protein fragment; and

(b) a second expression vector having a nucleic acid encoding a second protein selected from the group consisting of

- (1) HIV GAG polypeptide,
- (2) a HIV GAG polypeptide homologue having an amino acid sequence at least 90% identical to that of HIV GAG polypeptide and capable of interacting with Tsg101,
- (3) HIV GAGp6 protein,
- (4) a HIV GAGp6 homologue having an amino acid sequence at least 90%

identical to that of HIV GAGp6 polypeptide and capable of interacting with Tsg101,  
(5) a HIV GAGp6 fragment capable of interacting with Tsg101, and  
(6) a fusion protein containing said HIV GAG polypeptide, said HIV GAG polypeptide homologue, said HIV GAGp6 protein, said HIV GAGp6 homologue or said HIV GAGp6 fragment.

46. The host cell of Claim 45, wherein said host cell is a yeast cell.

47. The host cell of Claim 45, wherein said first and second proteins are expressed in fusion proteins.

48. The host cell of Claim 45, wherein one of said first and second nucleic acids is linked to a nucleic acid encoding a DNA binding domain, and the other of said first and second nucleic acids is linked to a nucleic acid encoding a transcription-activation domain, whereby two fusion proteins can be produced in said host cell.

49. The host cell of Claim 45, further comprising a reporter gene, wherein the expression of the reporter gene is determined by the interaction between the first protein and the second protein.

50. A host cell comprising:

(a) a first expression vector having a nucleic acid encoding a first protein which is selected from group consisting of

(i) Tsg101 protein,

(ii) a Tsg101 protein homologue having an amino acid sequence at least 90% identical to that of Tsg101 and capable of interacting with HIV GAGp6,

(iii) a Tsg101 protein fragment containing the Tsg101 UEV domain, and

(iv) a fusion protein containing said Tsg101 protein, said Tsg101 protein homologue or said Tsg101 protein fragment; and

(b) a second expression vector having a nucleic acid encoding a second protein selected from the group consisting of

- (1) a retrovirus GAG polypeptide having the P(T/S)AP late domain motif,
- (2) a homologue of said retrovirus GAG polypeptide, said homologue having an amino acid sequence at least 90% identical to that of said retrovirus GAG polypeptide and capable of interacting with Tsg101,
- (3) a fragment of said retrovirus GAG polypeptide, said fragment being capable of interacting with Tsg101, and
- (4) a fusion protein containing said retrovirus GAG polypeptide, said retrovirus GAG polypeptide homologue or said retrovirus GAG polypeptide fragment.

51. A method for providing a compound capable of interfering with an interaction between the first and second proteins in the protein complex of Claim 8 comprising:

providing atomic coordinates defining a three-dimensional structure of said protein complex; and

designing or selecting compounds capable of interfering with the interaction between said first protein and said second protein based on said atomic coordinates.

52. A method for providing a compound capable of interfering with an interaction between the first and second proteins in the protein complex of Claim 17 comprising:

providing atomic coordinates defining a three-dimensional structure of said protein complex; and

designing or selecting compounds capable of interfering with the interaction between said first protein and said second protein based on said atomic coordinates.

53. A method for providing a compound capable of interfering with an interaction between the first and second proteins in the protein complex of Claim 22 comprising:

providing atomic coordinates defining a three-dimensional structure of said protein complex; and

designing or selecting compounds capable of interfering with the interaction between said first protein and said second protein based on said atomic coordinates.

54. A method for selecting a compound capable of inhibiting a protein-protein interaction between Tsg101 and HIV GAGp6, comprising:

contacting a test compound with a protein selected from group consisting of

(i) Tsg101 protein,

(ii) a Tsg101 protein homologue having an amino acid sequence at least 90% identical to that of Tsg101 and capable of interacting with HIV GAGp6,

(iii) a Tsg101 protein fragment containing the Tsg101 UEV domain, and

(iv) a fusion protein containing said Tsg101 protein, said Tsg101 protein homologue or said Tsg101 protein fragment; and

determining whether said test compound is capable of binding said protein.

55. The method of Claim 54, further comprising testing a test compound capable of binding said protein for its ability to interfere with a protein-protein interaction between Tsg101 and HIV GAGp6.

56. The method of Claim 55, further comprising testing a test compound capable of binding said protein for its ability to inhibit HIV viral budding from an HIV-infected host cell.

57. A method for selecting a compound capable of inhibiting a protein-protein interaction between Tsg101 and HIV GAGp6, comprising:

providing atomic coordinates defining a three-dimensional structure of a protein selected from group consisting of

(i) Tsg101 protein,

(ii) a Tsg101 protein homologue having an amino acid sequence at least 90% identical to that of Tsg101 and capable of interacting with HIV GAGp6,

(iii) a Tsg101 protein fragment containing the Tsg101 UEV domain, and

(iv) a fusion protein containing said Tsg101 protein, said Tsg101 protein

homologue or said Tsg101 protein fragment; and

designing or selecting compounds capable of interacting with said protein based on said atomic coordinates.

58. The method of Claim 57, further comprising testing a compound capable of interacting with said protein for its ability to interfere with a protein-protein interaction between Tsg101 and HIV GAGp6.

59. The method of Claim 57, further comprising testing a test compound capable of interacting with said protein for its ability to inhibit HIV viral budding from an HIV-infected host cell.

60. An isolated antibody selectively immunoreactive with a protein complex comprising Tsg101 and HIV GAGp6.